## REMARKS

Claims 12-23 are pending in the present application. Claims 1-11 had been previously canceled. Claims 12 and 14 have been amended and claim 13, 21 and 23 have been canceled herein. Accordingly, claims 12, 14-20 and 22 will be pending upon entry of the instant amendment. Any cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite prosecution of the application. No new matter has been added, and Applicants submit that all of the claims are now in condition for allowance.

### *Specification*

The specification has been amended as follows:

1) The Related Applications section has been amended to include the status of the patent applications to which the present application claims priority; and
2) The zinc binding consensus sequence, i.e. $HEXXHX_{18}E$, disclosed on pages 4 and 9 of the specification has been added to the sequence listing as required by 37 C.F.R. 1.821-1.825. This sequence appears in the sequence listing as SEQ ID NO:8. The specification has therefore been amended to include the term "SEQ ID NO:8" in the corresponding paragraphs at pages 4 and 9.

### *Information Disclosure Statement*

The Examiner objected to the Information Disclosure Statement (IDS) that was filed on January 29, 2004 because citation numbers CA, CB, CE, CK, CL, CM, CO and CR were incomplete. Applicants have retrieved these records and re-submit them along with all of the required information, i.e. publication dates, in a new IDS enclosed herewith.

### *Compliance with Sequence Rules*

The Examiner objected to the specification as it contains amino acid sequences in excess of 3 amino acids that are not accompanied by a SEQ ID NO. Applicants have therefore included the zinc binding consensus sequence $HEXXHX_{18}E$ in the sequence listing as SEQ ID NO:8. Applicants have additionally amended the specification to include "SEQ ID NO:8" wherever this sequence appears in the specification. Applicants submit herewith a substitute computer readable form of the sequence listing as well as a substitute paper copy of the sequence listing.

Applicants submit that no new matter has been added by way of amendment and that the computer readable copy and paper copy of the substitute sequence listing submitted herewith introduce no new matter. Applicants respectfully request reconsideration of this objection.

***Claim Objections***

The Examiner objected to claim 18 because it contains the acronym ATCC. This acronym appears for the first time in claim 12a), hence Applicants have amended claim 12a) to read "American Type Culture Collection (ATCC)", thereby rendering the Examiner's objection moot.

The Examiner additionally objected to claims 21 and 23 due to the language used in the claims from which claims 21 and 23 depend. In order to expedite prosecution and in no way acquiescing to the Examiner's objection, Applicants have canceled claims 21 and 23, thereby rendering the Examiner's objections moot.

Applicants therefore respectfully request reconsideration and withdrawal of the objections to the claims.

***Rejection of Claims 12-14 and 19 under 35 U.S.C. §112, first paragraph***

Claims 12-14 and 19 were rejected under 35 U.S.C §112, first paragraph, "[a]s failing to comply with the written description requirement." Specifically, the Examiner states "[t]he instant specification does not describe the structural characteristics that allow a particular aminopeptidase to catalyze a specific reaction. Further, the specification does not describe the structural characteristics of SEQ ID NO:1 that limit its activity to N-terminal arginines and lysines. As such one of skill in the art could not conclude that Applicant was in possession of the genus of polypeptides comprising 90%-95% sequence identity to SEQ ID NO:1, and the ability to cleave any N-terminal amino acid from any polypeptide."

Applicants respectfully traverse this rejection, however in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have amended claims 12a) and 12b) to increase the % identity to 95% and Applicants have canceled claims 12c) and 13.

"The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'" *See Union Oil Co. v. Atlantic*

*Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000). In particular, an adequate description can be made by disclosing identifying characteristics, such as complete or partial structure, functional characteristics, or physical and/or chemical properties. "Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph 'Written Description' Requirement," 66 Fed. Reg. 1099 (January 5, 2001). An Applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id.*

As mentioned above, newly pending claims 12a) and 12b) recite polypeptides with at least 95% identity to the amino acid sequence of SEQ ID NO:1 or polypeptides encoded by nucleic acid sequences with at least 95% identity to the nucleotide sequence of SEQ ID NO:2, wherein the polypeptide further has aminopeptidase activity. The recitation of at least 95% sequence identity is a *very predictable structure* of the sequences encompassed by the claimed invention. The Examiner is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, polypeptides having at least 95% sequence identity to the sequence set forth in SEQ ID NO:1 or polypeptides encoded by nucleic acid sequences having at least 95% sequence identity to the sequence set forth in SEQ ID NO:2.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, or by means of a recitation of structural features common to the genus, which features constitutes a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997); see also Guidelines for Examination of Patent Applications under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001). The recitation of a

predictable structure of at least 95% sequence identity to SEQ ID NO:1 is sufficient to satisfy the written description requirement.

As indicated above, an applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. The claimed polypeptide variants are required to have aminopeptidase activity, thus the claims provide a functional characterization of the sequences claimed in the genus.

Example 14 of the Revised Interim Written Description Guidelines is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction A to B. The Training Materials concludes that the generic claim of Example 14 is sufficiently described under 35 U.S.C. §112, first paragraph, because 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus" and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A to B. The Guidelines conclude that one of skill in the art would recognize the necessary attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that newly pending claims 12a) and 12b), and dependent claims 14 and 19 therefrom, satisfy the written description requirements of 35 U.S.C. §112, first paragraph. Specifically, the claims of the present invention encompass polypeptide sequences having at least 95% sequence identity to the sequence of SEQ ID NO:1 or polypeptide sequences encoded by a nucleic acid sequence having at least 95% sequence identity to the sequence of SEQ ID NO:2, wherein the polypeptide has aminopeptidase activity. As in Example 14, the specification discloses the amino acid sequence of SEQ ID NO:1, and the claims recite a limitation requiring the compound to have a specific function (*i.e.*, aminopeptidase activity).

In summary, the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus would be clearly recognized by one of skill in the art and consequently, the Applicant has disclosed the necessary common attributes or features of the elements possessed by the members of the genus. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection over claims 12-14 and 19.

***Rejection of Claims 12-14, 18, 19 and 23 under 35 U.S.C. §112, first paragraph***

Claims 12-14, 18, 19 and 23 were rejected under 35 U.S.C §112, first paragraph, because "[t]he specification, while being enabling for a polypeptide comprising SEQ ID NO:1 or fragments of SEQ ID NO:1, wherein the fragments have the amino peptidase activity of SEQ ID NO:1, does not reasonably provide enablement for sequence variants of SEQ ID NO:1, or sequence variants of fragments of SEQ ID NO:1, wherein the variants have any aminopeptidase activity broadly."

Applicants respectfully traverse this rejection, however in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have amended claims 12a) and 12b) to increase the % identity to 95% and Applicants have canceled claims 12c) and 13.

The limitations within new claims 12a) and 12b) are fully enabled within the specification as Applicants have provided teachings for every element needed for one of skill in the art to practice the claimed invention.

Applicants have provided teachings on how to generate functional variants by performing conservative substitutions within the claimed polypeptide. As defined on page 13 of the specification, conservative amino acid substitutions are phenotypically silent. Applicants have also defined which of the amino acids may be conservatively substituted, thereby providing a skilled artisan the necessary tools to generate functional variants of the claimed polypeptide.

Applicants have additionally provided teachings for one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired aminopeptidase activity. As taught on, for example, pages 24 and 25 of the specification, beginning at line 24 of page 24, such an aminopeptidase activity can include "[e]xopeptidase activity for basic amino acids (lysine and/or arginine), dependence upon $Zn^{2+}$ for exopeptidase activity, leukotriene $A_4$ epoxide hydrolase activity, and the ability to be inhibited by classical aminopeptidase inhibitors such as bestatin and arphamenine." Based on these activities, Applicants further teach assays which can be useful for determining exopeptidase activity, such as "[c]leavage of $Arg^0$-Leu-enkephalin, $Arg^0$-Met-enkephalin, $Arg^1$-$Lys^6$-somatostatin-14, leukotriene $A_4 \rightarrow$ leukotriene $B_4$, the removal of basic amino acids from L-amino acyl β-naphthylamides, the removal of basic amino L-amino acid-7-amido-4-methylcoumarins, cleavage of lysine from the amino terminus of kallidins, $Arg^0$-neurokinin A, $Arg^0$-α-atrial natriuretic factor, and thymopentin." (refer to lines 1-7 of page 25).

Performing such assays to determine whether or not a variant having at least 95% identity to the sequence of SEQ ID NO:1 has the desired properties would not constitute undue experimentation. In fact, the Examiner concedes that the specification is enabling for polypeptide "[f]ragments of SEQ ID NO:1, wherein the fragments have the amino peptidase activity" (refer to page 6 of the Office Action). Applicants submit that if the specification is enabling for polypeptide fragments having aminopeptidase activity and that if performing assays to determine whether such fragments do in fact possess the desired activity, then performing assays to determine whether polypeptide variants have the desired activity is no less enabled as the work involved is essentially the same. Therefore, if performing the assays on polypeptide fragments does not constitute undue experimentation, then performing the assays on polypeptide variants should also not be undue experimentation.

Therefore, Applicants have provided all of the necessary information to enable one of skill in the art to generate variants having at least 95% identity to the sequence of SEQ ID NO:1 and to perform assays to determine whether or not the sequences generated do in fact have the desired aminopeptidase activity.

Therefore, contrary to the Examiner's assertions, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of newly pending claims 12, 14-20 and 22. Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection over claims 12, 14-20 and 22.

***Rejection of Claims 12-23 under 35 U.S.C. §112, first paragraph***

Claims 12-23 were rejected under 35 U.S.C §112, first paragraph, as failing to meet the enablement requirement. Specifically, the Examiner requests that Applicants submit an affidavit or declaration stating that the ATCC deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty.

Applicants submit herewith a Deposit Declaration stating that a plasmid containing a human cDNA insert for gene 2786 was deposited with the ATCC on December 15, 2000 under the terms of the Budapest Treaty and assigned ATCC® Accession Number PTA-2811 and that upon granting of a patent on the instant application, all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed and the deposit will be replaced if viable samples cannot be dispensed by the repository.

Reconsideration and withdrawal of the 35 U.S.C §112, first paragraph rejection over claims 12-23 is therefore respectfully requested.

***Rejection of Claims 12-14 and 19 under 35 U.S.C. §102(b)***

Claims 12-14 and 19 were rejected under 35 U.S.C §102(b), as being anticipated by Belhacene et al. (Eur. J. Immunol. 23(8), 1948-1955 (1993)) as evidenced by NCBI gi number 40316915. Specifically, the Examiner states that Belhacene anticipates the claims because Belhacene taught a purified human aminopeptidase based on NCBI gi number 40316915.

Applicants respectfully traverse the rejection and note that Belhacene et al. (Eur. J. Immunol. 23(8), 1948-1955 (1993)) do not disclose any sequence and as such, the publication is not anticipatory art under 102(b). Applicants also note that there have been three versions of RefSeq Accession Number NP_064601. For clarity, Applicants begin with the most recent version of this accession number, which corresponds to gi number 40316915, which was cited by the Examiner and which is included in the attached Supplemental Information Disclosure Statement (IDS) as citation D1:

1) gi:40316915 (NP_064601.3): The sequence disclosed under this gi number does not correspond to the first version of sequence which was uploaded in the NCBI database. Under the COMMENT section beginning on line 7 of page 2, there is a note stating that on December 23, 2003, this version of the sequence replaced gi:13443031 (refer to line 11 on page 2 of D1). Of note, the sequence disclosed in D1 corresponds to 650 amino acids in length.
2) gi:13443031 (NP_064601.2): Applicants submit this NCBI record herewith in the Supplemental IDS as citation D2. Again, the sequence disclosed under this gi number does not correspond to the first version of sequence which was uploaded in the NCBI database. Under the COMMENT section beginning on line 25 of page 1 (assuming that line 1 begins at LOCUS), there is a note stating that on March 24, 2001, this version of the sequence replaced gi:9910198 (refer to line 29 on page 1 of D2). Of note, the sequence disclosed in D2 corresponds to 657 amino acids in length.
3) gi:9910198 (NP_064601.1): Applicants submit this NCBI record herewith in the Supplemental IDS as citation D3. The sequence disclosed under this gi number does correspond to the first version of sequence which was uploaded in the NCBI database.

Of note, the sequence disclosed in this document is only 360 amino acids in length and it corresponds to the 3' end of the aminopeptidase molecule.

Therefore, since gi:9910198 was updated on March 24, 2001, which is well after the filing date of the present invention, and since the sequence disclosed in gi:9910198 corresponds to only a fragment of the aminopeptidase molecule of the present invention, Applicants submit that Belhacene et al. does not anticipate claims 12, 14 and 19. Reconsideration and withdrawal of the 35 U.S.C §102(b) rejection over claims 12-14 and 19 is respectfully requested.

## CONCLUSIONS

In view of the amendments and remarks made herein, Applicants respectfully submit that the rejections presented by the Examiner are now overcome and that this application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

This paper is being filed timely as a request for a one month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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